

FILING BY "EXPRESS MAIL" UNDER 37 CFR 1.10

EL 913014816 US  
Express Mail Label NumberNovember 20, 2001  
Date of Deposit

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

OKUNO ET AL.

APPLICATION NO:

FILED:

FOR: PHARMACEUTICAL COMPOSITIONS AND USES

Assistant Commissioner for Patents  
Washington, D.C. 20231PRELIMINARY AMENDMENT

Sir:

Prior to calculation of the filing fees, please amend the application as follows:

## IN THE SPECIFICATION

Under the Title and before the first line, please insert - -This is a continuation of International Application No. PCT/EP00/04562, filed May 19, 2000, the contents of which are incorporated herein by reference.- -

## IN THE CLAIMS

6. (Amended) A method according to claim 1, wherein the patient is suffering from inflammation, myocardial ischemia, rheumatoid arthritis, osteoarthritis and tumour growth, invasion or metastasis.

7. (Amended) A method according to claim 1, in which the bisphosphonate is selected from the following compounds or a pharmaceutically acceptable salt thereof, or any hydrate thereof: 3-amino-1-hydroxypropane-1,1-diphosphonic acid (pamidronic acid), 3-(N,N-dimethylamino)-1-hydroxypropane-1,1-diphosphonic acid, 4 amino-1-hydroxybutane-1,1-diphosphonic acid (alendronic acid), 1-hydroxy-ethidene-bisphosphonic acid, 1-hydroxy-3-(methylpentylamino)-propylidene-bisphosphonic acid, ibandronic acid, 6-amino-1-hydroxyhexane-1,1-diphosphonic acid,

T003T 2256860

3-(N-methyl-N-n-pentylamino)-1-hydroxypropane-1, 1-diphosphonic acid, -1-hydroxy-2-(imidazol-1-yl)ethane-1,1-diphosphonic acid; 1-hydroxy-2-(3-pyridyl)ethane-1,1-diphosphonic acid (risedronic acid), including N-methyl pyridinium salts thereof, for example N-methyl pyridinium iodides such as NE-10244 or NE-10446; 1-(4-chlorophenylthio) methane-1,1-diphosphonic acid (tiludronic acid), [e.g. tiludronate;] 3[N-(2-phenylthioethyl)-N-methylamino]-1-hydroxypropane-1,1-diphosphonic acid; 1-hydroxy-3-(pyrrolidin-1-yl)propane-1,1-diphosphonic acid, 1-(N-phenylaminothiocarbonyl)methane-1,1-diphosphonic acid, 5-benzoyl-3,4-dihydro-2H-pyrazole-3,3-diphosphonic acid tetraethyl ester, 1-hydroxy-2-(imidazo[1,2-a]pyridin-3-yl)ethane-1,1-diphosphonic acid, and 1,1-dichloromethane-1,1-diphosphonic acid (clodronic acid).

8. (Amended) A method according to claim 1, in which the bisphosphonate is pamidronic acid or zoledronic acid, or a pharmaceutically acceptable salt thereof, or any hydrate thereof.

#### Remarks

The claims have been amended to eliminate multiple dependencies. A marked-up version of the claims with markings to show changes made is attached hereto.

Early and favorable consideration of the application is respectfully requested.

Respectfully submitted,

  
Carol A. Loeschorn  
Attorney for Applicants  
Reg. No. 35,590

Novartis Corporation  
Patent and Trademark Dept.  
564 Morris Avenue  
Summit, NJ 07901-1027  
(908) 522-6932

Date: November 20, 2001

## **MARKED-UP VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE**

### **IN THE SPECIFICATION**

Under the Title and before the first line, please insert - - This is a continuation of International Application No. PCT/EP00/04562, filed May 19, 2000, the contents of which are incorporated herein by reference.- -

### **IN THE CLAIMS**

6. (Amended) A method according to claim 1 [or a use according to claim 2 or 3 for the treatment of angiogenesis in a] ,wherein the patient is suffering from inflammation, myocardial ischemia, rheumatoid arthritis, osteoarthritis and tumour growth, invasion or metastasis.
7. (Amended) A method according to claim 1 [or a use according to claim 2 or 3,] in which the bisphosphonate is selected from the following compounds or a pharmaceutically acceptable salt thereof, or any hydrate thereof: 3-amino-1-hydroxypropane-1,1-diphosphonic acid (pamidronic acid), [e.g. pamidronate (APD);] 3-(N,N-dimethylamino)-1-hydroxypropane-1,1- diphosphonic acid, [e.g. dimethyl-APD;] 4 amino-1-hydroxybutane-1,1-diphosphonic acid (alendronic acid), [e.g. alendronate;] 1-hydroxy-ethidene-bisphosphonic acid, [e.g.-etidronate;] 1-hydroxy-3-(methylpentylamino)-propylidene-bisphosphonic acid, ibandronic acid, [e.g. ibandronate;] 6-amino-1- hydroxyhexane-1,1-diphosphonic acid,[e.g. amino-hexyl-BP;] 3-(N-methyl-N-n-pentylamino)-1-hydroxypropane-1, 1-diphosphonic acid, [e.g. methyl-pentyl-APD (=BM 21,0955);]-1-hydroxy-2-(imidazol-1-yl)ethane-1,1-diphosphonic acid; 1-hydroxy-2-(3-pyridyl)ethane-1,1-diphosphonic acid (risedronic acid),[e.g. risedronate,] including N-methyl pyridinium salts thereof, for example N-methyl pyridinium iodides such as NE-10244 or NE-10446; 1-(4-chlorophenylthio) methane-1,1-diphosphonic acid (tiludronic acid), [e.g.tiludronate;]3[N-(2-phenylthioethyl)-N-methylamino]-1-hydroxypropane-1,1-diphosphonic acid; 1-hydroxy-3-(pyrrolidin-1-yl)propane-1,1-diphosphonic acid, [e.g. EB 1053 (Leo);] 1-(N-phenylaminothiocarbonyl)methane-1,1-diphosponic acid, [e.g. FR 78844 (Fujisawa);] 5-benzoyl-3,4-dihydro-2H-pyrazole-3,3-diphosphonic acid tetraethyl ester, [e.g. U-81581 (Upjohn);] 1-hydroxy-2-(imidazo[1,2-a]pyridin-3-yl)ethane-1,1-diphosphonic acid, [e.g. YM529; and 1,1-dichloromethane-1,1-diphosphonic acid (clodronic acid), [e.g. clodronate].
8. (Amended) A method according to claim 1 [or a use according to claim 2 or 3], in which the bisphosphonate is pamidronic acid or zoledronic acid, or a pharmaceutically acceptable salt thereof, or any hydrate thereof.